Ward et al. (2010) recommended that "the relationship between occupational exposure to carbon black and validated biomarkers of oxidative stress should be examined." Despite the appeal of biomarkers of oxidative stress in pinpointing inflammatory changes associated with malignant and nonmalignant illnesses, such markers are nonspecific, not well validated, and appear not "ready for prime time," as noted in a recent symposium on nanotoxicology (Fischman et al. 2011).

A meta-analysis of all three major carbon black cohorts (United States, United Kingdom, and Germany) to assess risk of heart disease is also under way. In a recent position paper, Brook et al. (2004) noted that particle exposure may play a role in the development of heart disease.

Ward et al. (2010) suggested evaluating carbon black particle size and surface area. However, the physical and chemical properties of untreated manufactured carbon blacks are distinctly different from ubiquitous carbon core particulates in both occupational and ambient atmospheres (Kuhlbusch and Fissan 2006). Approximately 90% of manufactured carbon black is used for tire and automotive rubber products. In products, such as toners, plastics, and surface coatings, carbon black is matrix-bound, and not an exposure risk to end-users. Care should be taken when applying quantitative models that claim to address the particle size and surface area topics (Tomenson and Morfeld 2010).

The authors serve as scientific advisors to the International Carbon Black Association (ICBA), a scientific, non-profit corporation originally founded in 1977, with the purpose of sponsoring, conducting, and participating in investigations, research, and analyses relating to the health, safety, and environmental aspects of the production and use of carbon black. This manuscript was neither influenced by the ICBA nor by any company funding the ICBA, nor does it present any view or opinion of the ICBA or of the companies. H.M. is president of Muranko and Associates, a consulting company that provides industrial hygiene and safety services and serves as expert witness in industrial safety cases.

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We appreciate the comments and additional information from McCunney et al. We are pleased to learn of the new epidemiological studies that are under way in the U.S. and E.U. carbon black cohorts. These studies may provide the opportunity to fill some of the research gaps discussed in our review (Ward et al. 2010). As mentioned by McCunney et al. in their letter, we recommend the collection of particle size–specific and quantitative exposure data, and the recruitment of additional facilities (Ward et al.). Studies in animals have shown relationships between the particle surface area dose of poorly soluble particles (including carbon black) in the lungs and biomarkers of oxidative stress and inflammation in rats and mice (Elder et al. 2005; Sager and Castranova 2009; Stoeger et al. 2006) and lung tumors in rats (Driscoll 1996; Heinrich et al. 1995; Nikula et al. 1995). Although these relationships with particle surface area dose have not been reported in human studies, exposure to carbon black by particle mass has been associated with respiratory effects including lung function decrements in workers (Gardiner et al. 2001).

Concerning biomarkers of oxidative stress, we think the epidemiology studies under way may provide an opportunity to investigate and test hypotheses about possible biomarkers of exposure and response to carbon black. As we discussed in our paper (Ward et al. 2010), although oxidative stress has been invoked as a mechanism in the carcinogenicity of a number of agents (including particles such as carbon black), methodological challenges to the validation of oxidative stress biomarker assays remain. To facilitate this process, guidelines have been developed to standardize the collection and measurement of oxidative stress biomarkers in humans (American Thoracic Society 1999; Horváth et al. 2005).

We look forward to further reports from the carbon black mortality studies, including exposure–response analyses, which could help fill important occupational health research gaps. Well-conducted epidemiologic studies will be particularly critical to inform carcinogen classification and risk assessment processes.

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